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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/787,279	02/26/2004	Patrick R. Connelly	034405-014	5157

21839 7590 08/24/2006

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POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/787,279	CONNELLY ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-26 and 32-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-26 and 32-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed January 24, 2006 is acknowledged and has been entered.

Election/Restrictions

2. Applicant's election without traverse of claims 17-30 in the reply filed on January 24, 2006 is acknowledged.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 17, 24-25, 29-30, and 35-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Guirguis (US 5,133,363).

Guirguis reference teaches that the shuttle resin/sample container 70 (i.e. assembly) is placed within sample collection apparatus 20 (i.e. second chamber), wherein the shuttle container comprises multiple, concentric, cylindrical chambers 77, 81, 85, and 87, each filled with a predetermined sequence of beads that covalently bind various antigens and antibodies, wherein chamber 77 is a control with unbound beads,

chamber 81 (i.e. third chamber disposed within first and second chamber; inner wall comprised to a target specific binding agent) has beads with either antigen A and anti-B antibody thereon, and chamber 85 (i.e. first chamber disposed within second chamber) has beads with either anti-B antibody or anti-A antibody thereon. See column 3, lines 13-16; column 4, lines 29-59; and Figures 1, 3, and 5-6. In addition, Guirguis teaches the step of pushing down the shuttle container such that a specimen sample fluid within the sample collection apparatus flows into the shuttle container and contacts the beads with ligands immobilized thereon (i.e. feeding a fluid into an assembly; introducing a first portion of the flow of the fluid to the first chamber, and a second portion of the flow of the fluid to the second chamber; inner wall is permeable to biological target) and captures through-antigen-antibody reaction the specific component of the fluid which is to be tested (i.e. allowing said target specific binding agent to bind with said biological target), wherein labeled primary antibodies are added to the sample fluid previous to the step of pushing down the shuttle container in order to for labeled antibody-antigen complexes. See column 5, lines 58-63 and column 6, lines 5-18; and Figures 7-8. Since Guirguis teaches that the fluid flows ***into*** the first and second chambers due to the motion of the plunger, the lower boundary of the shuttle resin/sample container necessarily has an inlet. Guirguis also teaches an outlet since the sample fluid flows ***completely through*** the container and into body cavity 53 (i.e. inlet and outlet at opposite ends of the assembly). See column 5, line 58 to column 6, line 4; and Figures 4 and 9. Furthermore, Guirguis teaches that the upper surface of disc membrane 100 on top of the shuttle container provides a surface upon which primary antibody and/or

antigen-antibody complexes are captured by secondary antibody immobilized on the membrane after flowing through the membrane from within the shuttle container (i.e. causing said biological target to migrate into a capture zone disposed within said second chamber). See column 6, lines 30-35.

With respect to claim 36, the interior of the first and second chambers are considered to be the claimed capture zone.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 18-19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guirguis (US 5,133,363) in view of Civin (US 4,714,680).

Guirgius reference has been disclosed above, but fails to teach that said biological target comprises a stem cell.

Civin reference teaches the step isolating hematopoietic stem cells by flowing blood through membranes having antibodies specific for the stem cells immobilized therein, in order to isolate the stem cells for therapeutic applications including bone marrow transplantation. See column 3, lines 11-19; and column 7, lines 9-14 and 45-52.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Guirguis with the step isolating hematopoietic stem cells by flowing blood through membranes having antibodies specific for the stem cells immobilized therein, as taught by Civin, in order to isolate the stem cells for therapeutic applications including bone marrow transplantation. In teaching the method of isolating hematopoietic stem cells, Civin teaches the advantage of collecting blood stem cells for

transplant into patients lacking stem cells, and provides motivation in collecting the stem cells using the method of Guirguis. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the step of isolating blood stem cells, as taught by Civin, in the method of Guirguis, since Guirguis teaches the flow of biological sample through membranes, and the stem cells of Civin can also flow through membranes.

With regards to claim 22, since Civin teaches isolating stem cells for transplantation, the cells would have to be removed from the solid phase membrane.

9. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guirguis (US 5,133,363) in view of Civin (US 4,714,680) as applied to claims 17 and 19 above, and further in view of Roberts (US 5,686,281).

Guirguis and Civin references have been disclosed above, but fail to teach that a morphological characteristic of said biological target is modified in such a way so as to differentiate said biological target.

Roberts reference teaches the introduction of chimeric constructs into hematopoietic stem cells, in order to permit the induction of effector functions such as differentiation to various cell types to provide a source of effector cells to fight virally infected diseases. See column 15, line 64 to column 16, line 27. Regarding the limitation "after the target specific binding agent binds with the biological target", since the step of Roberts requires that hematopoietic stem cells are available, it is necessarily

required that the step is performed after the capture of hematopoietic stem cells as taught by Guirguis and Civin.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Guirguis and Civin with the introduction of chimeric constructs into hematopoietic stem cells, as taught by Roberts, in order to permit the induction of effector functions such as differentiation to various cell types to provide a source of effector cells to fight virally infected diseases. The differentiation step taught by Roberts teaches the advantage of providing cells differentiated from stem cells to fight diseases, and provides motivation for differentiating the stem cells obtained by the method of Guirguis and Civin. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the differentiation step of Roberts in the method of Guirguis and Civin, since Guirguis and Civin teach the isolation of hematopoietic stem cells for therapeutic applications, and the differentiated cells of Roberts are derived from hematopoietic stem cells for the purpose of therapeutic applications.

10. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guirguis (US 5,133,363) in view of Daluge (US 5,399,580).

Guirguis reference has been disclosed above, but fails to teach that a morphological characteristic of said biological target is modified in such a way so as to devitalize the biological target.

Daluge reference teaches denaturing virus particles, in order to release HBV DNA strands for amplification and detection using polymerase chain reaction and a hybrid-capture assay, wherein the virus particles are captured by surface-coated antibodies. See column 13, lines 36-48. Regarding the limitation "after the target specific binding agent binds with the biological target", since the step of Daluge requires that virus particles are available, it is necessarily required that the step is performed after the capture of virus particles as taught by Guirguis and Civin.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Guirguis with the step of denaturing virus particles, as taught by Daluge, in order to release HBV DNA strands for amplification and detection using polymerase chain reaction and a hybrid-capture assay. The denaturing step of Daluge teaches the advantage of releasing DNA strands for PCR, and provides the motivation for performing the denaturing step on viral antigens obtained by the method of Guirguis. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a denaturing step, as taught by Daluge, in the method of Guirguis, since Guirguis teach the capture of antigen by antibodies, and the virus particles of Daluge are also able to be captured by antibodies.

11. Claims 23, 26, and 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guirguis (US 5,133,363) in view of Civin (US 4,714,680) as applied to claims 17-18 above, and further in view of Ameer et al (US 6,099,730).

Guirguis and Civin references have been disclosed above, but fail to teach that the inner chamber has a permeable wall with a size of at least 1 micron.

Ameer et al reference teaches a porous outer surface of an inner cylinder disposed within an outer cylinder, wherein pores are in the range of 0.2-3 μm, in order to provide a means for allowing capture of blood analytes within the inner cylinder and also allowing for an output of blood free of the analytes for detoxification or purification purposes. See column 2, lines 3-26; column 6, lines 40-48; and Figure 1.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Guirguis and Civin with a porous membrane in the range of 0.2-3 μm comprising the surface of the inner cylinder, as taught by Ameer et al, in order to provide a means for allowing capture of blood analytes within the inner cylinder and also allowing for an output of blood free of the analytes for detoxification or purification purposes. The advantage of being able to filter and purify blood provides the motivation to combine the porous membrane of Ameer et al with the method of Guirguis and Civin. In addition, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in including a porous membrane, as taught by Ameer et al, in the method of Guirguis and Civin, since Guirguis and Civin teach the capture of analytes in an chamber by providing a flow of fluid through the chamber, and the porous membrane of Ameer et al is also on an inner chamber in which fluid flows through it.

With respect to claim 33, Ameer et al teach a pump connected to reactor 10 that accepts bodily fluid from the device and outputs it back into the body. See column 9, lines 4-10 and Figure 5.

With respect to claim 34, Ameer et al teach that chamber 34 in outer cylinder 12 is free of active species (i.e. defines a hollow path). See column 8, lines 13-15; and Figures 1 and 3.

12. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guirguis (US 5,133,363) in view of Kaiser et al (WO 00/68689).

Guirguis reference has been disclosed above, but fails to teach that said third chamber has an inner wall comprised of a target specific binding agent.

Kaiser et al reference teaches multiple zones (i.e. chambers) in sequence, wherein each zone comprises a separate binding molecule, in order to perform cellular enrichment or purification of a particular subset of cells. See page 12, line 33 to page 13, line 1; and page 13, line 35 to page 14, line 10.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Guirguis with multiple zones (i.e. chambers) in sequence, wherein each zone comprises a separate binding molecule, as taught by Kaiser et al, in order to perform cellular enrichment or purification of a particular subset of cells. The sequential placement of chambers, as taught by Kaiser et al, teaches the advantage of sequential purification or cellular enrichment, which is the motivation for enriching cells using the apparatus taught in the method of Guirguis. In addition, one of

ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including multiple zones in sequence, as taught by Kaiser et al, in the method of Guirguis, since Guirguis teach the capture of antigen using antibodies in chambers, and the multiple zones of Kaiser et al are chambers that include capture agents.

13. Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guirguis (US 5,133,363) in view of Silver et al (US 7,006,858 B2).

Guirguis reference has been disclosed above, but fail to teach the step of implanting the assembly in a biological organism.

Silver et al reference teaches the implementation of a sensor within a blood vessel, wherein the sensor is an immunosensor, in order to continuously monitor a particular analyte in blood for an extended period of time. See abstract; column 2, lines 50-56; and column 26, line 50 to column 27, line 6.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Guirguis with the implementation of the sensor within a blood vessel, as taught by Silver et al, in order to continuously monitor a particular analyte in blood for an extended period of time. The advantage of being able to take multiple readings non-invasively provide the motivation to combine the in vivo implementation, as taught by Silver et al, in the method of Guirguis. In addition, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in including the step of Silver et al into the method of Guirguis,

since Guirguis teach a device that is capable performing specific binding, and the step of Silver et al allows for immunosensors to be placed in vivo.

Response to Arguments

14. Applicant's arguments in the Remarks section of the response filed January 24, 2006 have been fully considered but they are not persuasive.

On pages 8-10, Applicants traverse the anticipatory and obviousness rejections in the previous Office action. Applicants specifically make the following arguments:

(1) Applicants contend that Guirguis fails to disclose the step of modifying the flow dynamics of fluid by introducing a first portion of the flow into a first chamber, and introducing a second portion of flow into the second chamber. See page 8, 2nd paragraph.

(2) Applicants contend that Guirguis fails to teach an inlet and an outlet since Guirguis teaches that sample is kept in a secured contained condition after transport of the liquid. See page 8, last paragraph spanning page 9, 1st paragraph.

Applicants' arguments have been fully considered, but are not persuasive. With respect to Applicants' first argument above, the specification does not provide a detailed account on how the fluid is split into first and second portions. The specification only discloses that blood can be divided between different chambers, and that bodily fluid

can enter a multiplicity of chambers, but does not provide the mechanism in which this occurs. See page 33, lines 8-11; page 34, line 19; and Figures 14-15. Although Figures 14-15 are referenced, these figures only provide a flow chart with the same broad disclosure as the text. Therefore, in terms of the scope of the invention, as long as the prior art teaches different portions of the same liquid being split into different chambers, the step is anticipated. Since it has been shown that Guirguis provides a device with concentric chambers that are pushed into a fluid sample, it is necessarily required that different portions of the liquid each enter separate chambers. In addition, since the chambers are pushed into the fluid sample, the fluid is essentially forced upward through the chambers and is considered to move in a flowing fashion. Guirguis thereby provides adequate teaching to anticipate the instant step.

With respect to Applicants' second argument above, the argument refers to column 6, lines 36-41 of Guirguis reference. In examining the cited text, it is noted that the secured sample is within chamber 53 of transporter assembly 50, which is ***separated*** from the shuttle resin/sample container 70. See column 5, line 68 to column6 , line 4. Applicants are directed to the anticipation rejection in the previous Office Action and reapplied supra, which indicates that only the shuttle resin/sample container 70 is considered to be the claimed assembly. Therefore, since container 70 is separated from chamber 53 after pushing the container 70 through transporter assembly 50, and since fluid has to pass completely through container 70 in order to enter chamber 53, it is necessarily required that there is both an inlet and an outlet to

the container 70. Contrary to Applicants' claim that liquid is kept within the container 70, Guirguis clearly teaches the presence of an inlet and an outlet.

In light of the statements above, the previous anticipation rejection of claims 17, 24-25, and 29-30 are maintained.

15. On pages 9-10, Applicants' argue that the combination of Guirguis with a plurality of secondary references fails to teach the claimed step of modifying the flow dynamics of fluid introduced into the first and second chambers, and fails to teach an inlet and outlet.

Applicants' arguments have been fully considered, but are not persuasive. As established above, Guirguis fully anticipates the allegedly untaught limitations. Therefore, the secondary references are not required to re-teach the limitations.

In light of the statement above, Applicants' arguments are not persuasive and the dependent claims not covered under the anticipation rejection supra are found obvious over Guirguis in view of the applied secondary references.

Conclusion

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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